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Reply to the Letter to the Editor on "Co-prescription of Antiepileptic Drugs and Contraceptives"

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Letters to the Editor

Comment on research article: “Co-prescription of Antiepileptic Drugs and Contraceptives”

To the Editor:

The issue raised by Wang et al. [1] is of vital importance in avoiding unintended pregnancies and highlights the need for initial and continuing updating for prescribers of antiepileptic drugs and contraception.

In the UK, there is only one combined oral contraceptive pill containing 50 mcg of an estrogen (Norinyl-1). This preparation contains mestranol, a pro-drug partly metabolized to ethinylestradiol, which means that the potency of Norinyl-1 is roughly equivalent to that of a 30-mcg ethinylestradiol pill. It is recommended by the Clinical Effectiveness Unit of the Faculty of Sexual and Reproductive Healthcare of the Royal College of Obstetricians and Gynaecologists [2] that to achieve adequate circulating levels of ethinylestradiol, women taking enzyme-inducing drugs should be given one tablet of a 20-mcg plus one 30-mcg preparation, or two 30-mcg pills together daily (outside the product license), together with shortening the pill-free interval to 4 days or using extended regimens. Therefore, depending on the level of detail, the UK prescribing data do not always allow accurate determination of the dose actually taken. We wonder if this practice is also common in the Netherlands and if it was possible to identify this amongst the data for prescription of low-dose pills?

There seems to be no distinction in the paper between the different types of oral contraceptive or other methods of combined hormonal contraception such as the patch or vaginal ring. Combined hormonal oral preparations are the focus of the paper. There is arguably even greater concern about the situation for progestogen-only oral contraception and subdermal progestogen-only implants, where advice in the UK is to use alternative methods when enzyme-inducing medication is co-administered.

Lamotrigine, whilst listed as enzyme inducing, does not appear to have any effect on contraceptive effectiveness, but is not recommended to be used together with combined hormonal contraception as its levels may fluctuate on initiating and discontinuing the contraceptive during the hormone-free week, leading to reduction in seizure control and drug toxicity [2].

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- [1] Wang H, Bos JH, Lolkje TW, et al. Co-prescription of antiepileptic drugs and contraceptives. *Contraception* 2012;85:28–31.
- [2] Drug Interactions with Hormonal Contraception. Clinical Effectiveness Unit of the Faculty of Sexual and Reproductive Healthcare — clinical guidance, Jan 2011, updated Jan 2012 ISSN 1755-103X. <http://www.fsrh.org/pdfs/CEUGuidanceDrugInteractionsHormonal.pdf> accessed 15.1.12.

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To the Editor:

We appreciate the valuable comments by Elliman and Melvin, especially their reference to the Faculty of Sexual and Reproductive Healthcare Clinical Guidance of 2011 and update of 2012 [1], which were not yet available to us at the time of the submission of our manuscript.

Our analysis was based on pharmacy dispensing data over the year 2006; at that time, there was no guideline to prescribe two low-dose estrogen contraceptive pills to women using enzyme-inducing antiepileptic drugs, and this kind of prescription method was not practiced. We have checked the prescription database of the year 2006 and found only one

woman who was dispensed a combination two low-dose oral estrogen contraceptives.

We agree that progestogen-only oral contraception is of concern among enzyme-inducing antiepileptic drug users. This practice is rare in the Netherlands; in our 2006 pharmacy dispensing database, we found that less than 0.5% of all women of fertile age (i.e., irrespective of concomitant use of any medication) were on progestogen-only oral contraception. Therefore, we did not analyze our data for this specific combination.

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- [1] Clinical Effectiveness Unit of Faculty of Sexual and Reproductive Healthcare. Drug Interactions with Hormonal Contraception - Clinical Guidance, Jan 2011, updated Jan 2012, ISSN 1755-103X. <http://www.fsrh.org/pdfs/CEUGuidanceDrugInteractionsHormonal.pdf>. accessed Jan 15, 2012.